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# (54) Determining hypersensitivity of the respiratory system

(57) Apparatus, for determining airway hypersensitivity, has a duct 24 having a mouthpiece 22 at one end means 10 for producing sequential aerosol doses of bronchoconstrictor and bronchodilator, the aerosol producing means 10 communicating with the duct 24, means 12, e.g. a loudspeaker system, at the end of the duct 24 remote from the mouthpiece 22 for generating sinusoidal pressure waves in the duct, pressure gauge 30 for sensing the pressure in the duct at a zone adjacent to the mouthpiece, a vent 26 for expired air between the gauge and the aerosol-producing means, a pneumo-tachograph 28 for measuring the rate of air flow between the aerosol-producing means 10 and the means 12 for generating sinusoidal pressure waves, and means (32, 34, 36, 38) for calculating respiratory resistance from the measurements of air pressure, and flow rate, and displaying same.

FIG. 1

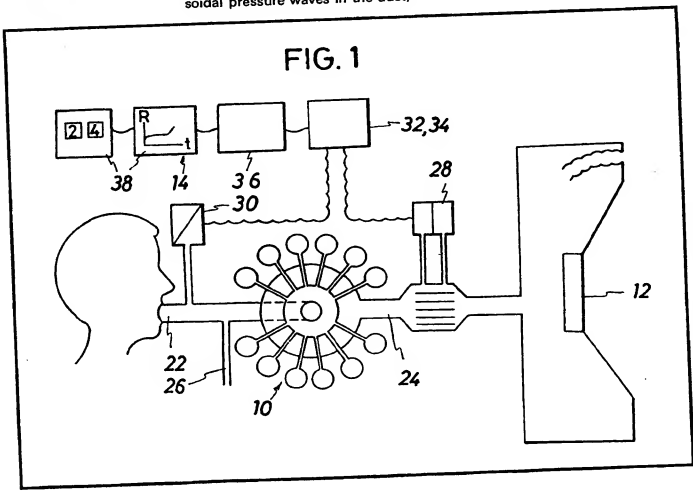


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FIG. 1

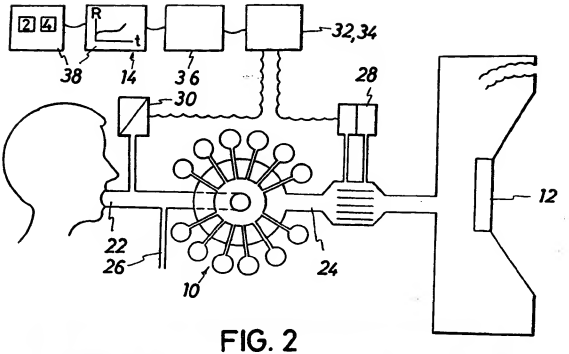


FIG. 2

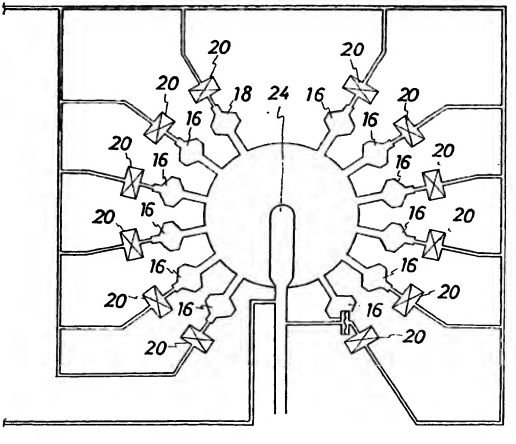

FIG. 3

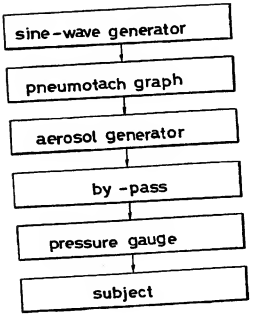


FIG. 4

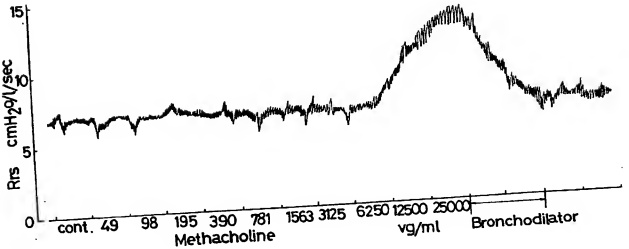

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FIG. 5

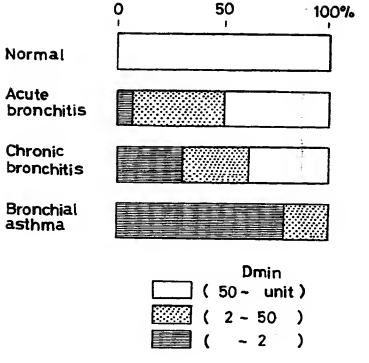
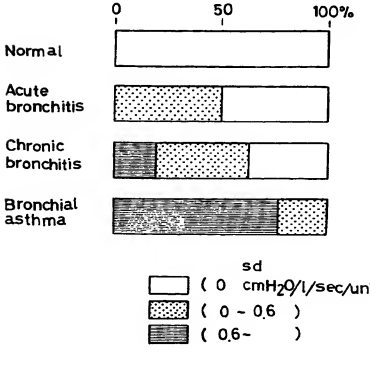



FIG. 6



SPECIFICATION

**Improvements in apparatus for determining hypersensitivity of the respiratory system**

The present invention relates to apparatus for determining airway hypersensitivity, in connection with the diagnosis of pulmonary diseases in human beings.

It is known that the origin of some chronic pulmonary diseases, particularly bronchial asthma, is a narrowing of the respiratory tract caused by hypersensitivity of it. Therefore, it is important to determine airway hypersensitivity for proper diagnosis and therapeutic treatment of pulmonary diseases.

Several techniques have been developed for determining airway hypersensitivity.

One such technique involves measuring the response of a subject to inhaled antigen spray. But this method has the shortcoming that quantitative analysis is not possible.

Another technique requires that the subject perform a forced expiration after inhaling a dose of broncho-constrictor in aerosol form. The concentration of the dose is gradually increased in order to determine the threshold of responsiveness, e.g. at what dose a 15% or 20% decrease in the forced expiration rate occurs.

This method has several defects namely; (1) the measurement is time-consuming because of the complicated and discontinuous procedures involved; (2) considerable effort by the subject is needed for forced expiration which itself induces broncho-constriction and so modifies the degree of broncho-constriction caused by inhalation of the broncho-constrictor; (3) the airway has a tendency to react to the stimulus in inhaling the drug in aerosol form and measuring the rate of forced expiration; (4) it is unsuitable for screening tests involving large numbers of people.

It has now been found that forced expiration is not desirable as part of a method for determining airway hypersensitivity. When testing pulmonary functions, the airway resistance, the pulmonary resistance and the respiratory resistance may be measured. The determination of airway hypersensitivity may be effected by measuring the change of airway resistance only. However, for clinical reasons, measurement of respiratory resistance is easier than that of airway resistance; respiratory resistance approximates to airway resistance and the measurement of respiratory resistance does not need abnormal effort from the subject.

According to the invention, there is provided apparatus for determining airway hypersensitivity comprising a duct through which the subject breathes, means for generating drug doses in aerosol form and of different concentrations, said generating means communicating with the duct, means for generating sinusoidal pressure waves in the duct, means for measuring air flow rate and pressure in the duct, and means for calculating respiratory resistance from these measurements.

Further according to the invention, there is provided apparatus for determining airway hypersensitivity comprising a duct having a mouthpiece at one end portion, means for producing sequential doses of bronchoconstrictor at different concentrations and bronchodilator in aerosol form, said aerosol-producing means communicating with the duct, means situated at the end of the duct remote from the mouthpiece for generating sinusoidal pressure waves in the duct, pressure sensing means for sensing the pressure in the duct at a zone adjacent to the mouthpiece, a vent for expired air between the pressure-sensing means and the aerosol producing means, means for measuring the rate of air flow between the aerosol-producing means and the means for generating sinusoidal pressure waves, and means for continuously calculating respiratory resistance from the measurements of air pressure, and flow rate, and displaying same.

When using the apparatus the subject inhales doses of bronchoconstrictor in aerosol form, of progressively higher concentrations and the respiratory resistance is continuously calculated by the oscillation method. When the resistance reaches twice its initial value, at which point the subject may show signs of dyspnoea, a bronchodilator is administered in aerosol form in order to measure the recovery rate of the respiratory resistance.

An embodiment of the invention will now be described, by way of example only, with reference to the accompanying diagrammatic drawings, in which:

*Figure 1* shows schematically an embodiment of apparatus for determining airway hypersensitivity, according to the present invention;

*Figure 2* shows schematically means for generating drug doses of different concentrations;

*Figure 3* is a block diagram showing the structure of apparatus;

*Figure 4* is a graph of respiratory resistance against bronchoconstrictor dosage; and

*Figures 5 and 6* are bar charts showing clinical results obtained when using the apparatus.

As shown in Fig. 1, the apparatus for determining hypersensitivity according to the present invention comprises means 10 for automatically generating drug doses in aerosol form, and of different concentrations, means 12 comprising a loud speaker system for generating sinusoidal pressure waves and means 14 for calculating the respiratory resistance from continuous measurements of mouth pressure and flow rate, made by pres-

sure-sensing means in the form of a pressure gauge 30, and pneumotachograph 28 respectively.

As shown in Fig. 2, the means 10 for generating drug doses in aerosol form comprises aerosol generators 16 for bronchoconstrictor at different concentrations and an aerosol generator 18 for a bronchodilator 18. An electromagnetic valve 20 is associated with each generator 16, 18, the valves 20 being opened by an electric circuit (not shown) in a sequence which releases bronchoconstrictor doses of progressively higher concentration. Each generator 16, 18 is at an equal distance from a duct 24 which connects the means 12 for generating sinusoidal pressure waves and mouthpiece 22, in order that the drug doses reach the mouthpiece in the same time.

To generate drug doses in aerosol form, the generators 16, 18 may operate by compressed air or by ultra-sonic waves for example. In each case the plurality of generators 16, 18 should be equidistant from the duct 24. A bypass 26 for ventilating carbon dioxide exhaled by the subject during the test is provided between the subject and the generating means 10.

The means 12 for generating sinusoidal pressure waves comprises a loudspeaker, an amplifier, and pressure generator, and in the preferred embodiment is adjusted to generate a pressure wave 3Hz which impinges on the lungs of the subject and is not influenced by the spontaneous breathing of the subject. The flow rate is measured by a pneumo-tachograph 28 in the form of a differential transducer which is provided between the generating means 10 and 12. The mouth pressure of the subject is measured by the pressure gauge 30 which is provided near the mouthpiece 22.

The calculating means 14 comprises an amplifier 32, a filter 34, a computer 36 and a display 38. It functions by recording the waves produced by quiet breathing and the sinusoidal wave pressure using the pneumotachograph 28 and pressure gauge 30 to measure the flow rate and the mouth pressure respectively. The signals corresponding to the reflected sinusoidal wave pressure are then separated out by the filter 34 and the ratio of amplitude of the reflected sinusoidal wave pressure to that of the flow rate, namely the respiratory resistance, is shown on the display 38.

The sequence of operation of the apparatus will now be described with reference to the block diagram of apparatus shown in Fig. 3.

The subject is positioned so that respiration occurs via the apparatus. As the subject inhales, sinusoidal pressure waves of constant amplitude are generated in the air flow by the loudspeaker 12. The flow rate is measured by the pneumo-tachograph 28 provided in the duct 24. The means 10 for generating drug doses in aerosol form then releases a dose into the airflow. Thus, the air inhaled by the subject carries a dose of bronchoconstrictor or bronchodilator in aerosol form, and sinusoidal pressure waves. The pressure of the expired air from quiet breathing is measured by pressure gauge 30 and vented by means of bypass 26. The calculating means 14 calculates the respiratory resistance from continuous measurements of flow rate and mouth pressure, and the instantaneous value of respiratory resistance is shown on the display 38.

Fig. 4 shows a typical response curve of respiratory resistance, as doses of bronchoconstrictor, and bronchodilator are administered. The abscissa is calibrated to show the concentration of bronchoconstrictor (metacholine) with serial dilution of equal volumes. The ordinate is calibrated to show respiratory resistance of the subject, as each dose of bronchoconstrictor is administered at one minute intervals. It is apparent from the graphs that as bronchoconstrictor is inhaled in doses of progressively higher concentration, the respiratory resistance remains constant until at a certain concentration it increases rapidly. The generator 18 for bronchodilator is then actuated, and the subject inhales the bronchodilator which reduces the respiratory resistance to a steady value.

The following parameters are of relevance in considering the response curve of respiratory resistance obtained with the apparatus hereinbefore described.

(A) Primary value of resistance: Resistance value during inhalation of saline solution in aerosol form.

(B) Threshold of responsiveness: The concentration of bronchoconstrictor at which the resistance starts to increase, or the cumulative dose up to the point at which the resistance starts to increase.

(C) Rate of increase of resistance: A measure of this is the ratio of increased resistance to the amount of medication, the increased resistance being measured after inhaling for two minutes from the moment at which the resistance starts to increase.

(D) Recovery rate: Recovery rate of respiratory resistance when subject inhales bronchodilator.

(E) Final value of resistance: Steady resistance value after recovery.

In Figs. 5 and 6, clinical results of determining airway hypersensitivity using the apparatus described are shown. The subjects consist of 8 with normal health, 14 suffering from acute bronchitis, 16 suffering from chronic bronchitis and 60 suffering from bronchial asthma. The distribution of primary value of resistance is shown in Fig. 5 by percentage. In Fig. 6, the distribution of increasing rate of resistance is shown, also by percentage.

In healthy subjects, an increase of respira-

tory resistance cannot be detected until they have inhaled a cumulative dose of 50 units. In contrast, the increase can be recognized in 50% of subjects with acute bronchitis, 63% of those with chronical bronchitis and 100% of those with bronchial asthma. From Fig. 6 is it apparent that the rate of change of resistance varies depending on which pulmonary disease the subject is suffering from.

With results obtained from the apparatus described definite distinctions can be recognized between pulmonary diseases such as bronchial asthma, chronical bronchitis and acute bronchitis, since the parameters A–E described above vary differently according to the disease. Thus the apparatus described may be used to diagnose pulmonary disease on the basis of airway hypersensitivity.

The preferred embodiment of the apparatus as described above, allows the respiratory resistance to be determined during quiet breathing and without undue effort from the subject, and the test can be completed in a short time. The apparatus can be easily operated and enables the operator to detect a change in the respiratory resistance immediately.

In addition the preferred apparatus does not induce spasmodic bronchial asthma, and thus it is possible to obtain a stable responsive curve.

CLAIMS

1. Apparatus for determining airway sensitivity, comprising a duct through which the subject breathes, means for generating drug doses in aerosol form and of different concentrations, said generating means communicating with the duct, means for generating sinusoidal pressure waves in the duct, means for measuring air flow rate and pressure in the duct, and means for calculating respiratory resistance from these measurements.

2. Apparatus according to claim 1, wherein the means for generating drug doses in aerosol form comprises a plurality of aerosol generators located equidistantly from a mouthpiece of the apparatus, and an electromagnetically actuated valve associated with each generator.

3. Apparatus according to claim 1 or claim 2, in which the aerosol generating means is operable under the action of ultrasonic means or compressed gas.

4. Apparatus according to any one of the preceding claims, in which the means for generating sinusoidal pressure waves includes a loudspeaker.

5. Apparatus according to any one of the preceding claims, which further comprises a vent for expired air opening out of the duct.

6. Apparatus according to any one of the preceding claims, when in use, wherein the means for generating drug doses in aerosol form is operative to provide bronchoconstrictor at various concentrations and a bronchodilator.

7. Apparatus for determining airway hypersensitivity comprising a duct having a mouthpiece at one end portion, means for producing sequential doses of bronchoconstrictor at different concentrations and bronchodilator in aerosol form, said aerosol producing means communicating with the duct, means situated at the end of the duct remote from the mouthpiece for generating sinusoidal pressure waves in the duct, pressure sensing means for sensing the pressure in the duct at a zone adjacent to the mouthpiece, a vent for expired air between the pressure-sensing means and the aerosol-producing means, means for measuring the rate of air flow between the aerosol-producing means and the means for generating sinusoidal pressure waves, and means for continuously calculating respiratory resistance from the measurements of air pressure, and flow rate, and displaying same.

8. Apparatus substantially as hereinbefore described with reference to the accompanying drawings.

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